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☐ 1: J Biol Chem 1992 Jun 25;267(18):13073-8

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The epithelin precursor encodes two proteins with opposing activities on epithelial cell growth.

Plowman GD, Green JM, Neubauer MG, Buckley SD, McDonald VL, Todaro GJ, Shoyab M.

Bristol-Myers Squibb Pharmaceutical Research Institute,
Seattle, Washington 98121.

Epithelin 1 and 2 were originally purified from rat kidneys based on their ability to inhibit the growth of A-431 human epidermoid carcinoma cells (Shoyab, M., McDonald, V.L., Byles, C., Todaro, G.J., and Plowman, G.D. (1990) Proc. Natl. Acad. Sci. U.S.A. 87, 7912-7916). This study presents the complete amino acid sequence of these two growth factors and the cloning of their cDNA from rat, mouse, and human sources. Epithelins 1 and 2 are 56- and 57-amino acid polypeptides, respectively, and share 47% amino acid sequence identity with the conserved spacing of 12 cysteine residues. Molecular cloning revealed that both proteins are encoded by a single precursor that contains 7 1/2 copies of this novel 12-cysteine motif, 2 of which represent the known active molecules. Recombinant expression in COS cells demonstrated that the epithelin 1 protein was mitogenic on rodent keratinocytes and fibroblasts. In contrast, epithelin 2 had no activity on these cells, but at high concentrations was capable of antagonizing the growth proliferative activities of epithelin 1. Northern analysis shows the epithelin mRNA to be expressed in many types of epithelial cells. The broad expression profile of epithelin transcripts, along with the opposing activities of the two mature protein products, implicates these factors as natural mediators of epithelial homeostasis.

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